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# BMJ Open

## Decreasing referrals to Transient Ischemic Attack clinics during the COVID-19 outbreak. Results from a multi-centre cross-sectional survey.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-041514
Article Type:	Original research
Date Submitted by the Author:	10-Jun-2020
Complete List of Authors:	D'Anna, Lucio; Imperial College London, Brain Sciences Sheikh, Ambreen; West Middlesex University Hospital, Stroke Bathula, Raj; Northwick Park Hospital, Stroke Elmamoun, Salwa; Chelsea and Westminster Healthcare NHS Trust, Stroke Oppong, Adelaide; Chelsea and Westminster Healthcare NHS Trust, Stroke Singh, Ravneeta; Chelsea and Westminster Healthcare NHS Trust, Stroke redwood, Rebecca; Chelsea and Westminster Healthcare NHS Trust, Stroke Janssen, John; Chelsea and Westminster Healthcare NHS Trust, Stroke Banerjee, Soma; Imperial College London, Brain Sciences vasileiadis, evangelos; Hillingdon Hospital, Stroke
Keywords:	STROKE MEDICINE, PREVENTIVE MEDICINE, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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# Decreasing referrals to Transient Ischemic Attack clinics during the COVID-19 outbreak.

## Results from a multi-centre cross-sectional survey.

Lucio D'Anna MD, PhD<sup>1,2</sup>, Ambreen Ali Sheikh MD<sup>3</sup>, Raj Bathula MD<sup>4</sup>, Salwa Elmamoun MD<sup>5</sup>, Adelaide Oppong MD<sup>5</sup>, Singh Ravneeta MD<sup>5</sup>, Rebecca Redwood MD<sup>5</sup>, John Janssen MD<sup>5</sup>, Soma Banerjee MD<sup>1,2</sup>, Evangelos Vasileiadis MD<sup>6</sup>.

<sup>1</sup>Department of Stroke and Neuroscience, Charing Cross Hospital, Imperial College London NHS Healthcare Trust, London, United Kingdom;

<sup>2</sup>Department of Brain Sciences, Imperial College London, London, United Kingdom;

<sup>3</sup>Stroke Centre, West Middlesex University Hospital, London, United Kingdom;

<sup>4</sup>Stroke Centre, Northwick Park Hospital, London, United Kingdom;

<sup>5</sup>Stroke Centre, Chelsea and Westminster Hospital, London, United Kingdom;

<sup>6</sup>Stroke Centre, Hillingdon Hospital, London, United Kingdom.

**Corresponding author:** Lucio D'Anna, Stroke Centre, Department of Stroke & Neurosciences, Charing Cross Hospital, Imperial College Healthcare NHS Trust, Fulham Palace Road, London W6 8RF, UK.

**Word count:** 1209

**Keywords:** COVID-19, transient ischemic attack, stroke prevention, TIA clinic

**Total number of tables and figures:** Figure 1

**Subject terms:** Transient Ischemic Attack

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**Abstract**

**Objective.** The COVID-19 pandemic is having major implications for stroke care with documented significant fall in hospital acute stroke admissions. We investigated whether COVID-19 has resulted in a decreased number of referrals to the Transient Ischemic Attack (TIA) clinics across the North West London region.

**Setting and Design.** All the TIA clinical leads of the North West London region received an invitation by email to participate in an online survey in May 2020. The survey questionnaire aimed to assess the number of patients with suspected TIA consecutively referred to each of the TIA clinics of the North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020, the COVID-19 period, and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019.

**Results.** We had a response rate of 100%. During the COVID-19 period, the TIA clinics of the North West London region received 440 referrals compared to 616 referrals received between 1<sup>st</sup> March to 30<sup>th</sup> April 2019 with a fall in the number of the referrals by 28.6%. In April 2020 compared with April 2019, the number of the referrals declined by 40.1%.

**Conclusions.** This multicentre analysis documented a significant reduction in the number of patients referred with suspected TIA to the specialised rapid outpatient clinics in the North West London region during the COVID-19 pandemic. Future studies are needed to confirm our findings and to better characterise the incidence of cerebrovascular disease during the COVID-19 pandemic.

### Strengths and Limitations of this study

- The first survey specifically in patients with Transient Ischemic Attack (TIA) clinics rather Stroke Units during the COVID-19 pandemic
- Participants are TIA clinical leads with insight into their service
- Response rate of 100%
- Reflection of results within the National Health Service in North West London region that might not be generalised to all international healthcare practices

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**Introduction**

Transient Ischemic Attack (TIA) is a common neurologic emergency that is strongly associated with a high early risk of subsequent stroke and therefore an urgent assessment and management of patients in a dedicated TIA clinic is considered to be critical to reduce significantly the 90-day stroke risk by almost 80%<sup>1-3</sup>.

A recent WSO survey across multiple countries including UK, Italy, Belgium, Greece, Iran, Chile and Colombia has documented that the COVID-19 pandemic has affected the stroke care with a significant fall in the number of stroke admissions, up to 80%, during the COVID-19 outbreak<sup>4</sup>. Moreover, preliminary data suggested that a smaller proportion of patients with milder stroke symptoms presented to hospital during the COVID-19 pandemic<sup>5</sup>. However, to date, it is unclear if COVID-19 pandemic has impacted on the number of referrals to the TIA clinics. In this observational multi-centre survey, we compared the number of patients with suspected TIA referred to all the TIA clinics across the North West London region during the COVID-19 pandemic compared with a similar period in 2019.

**Methods**

We conducted a multi-centre, cross-sectional survey in May 2020 to assess the impact of the current COVID-19 pandemic on the number of patients with suspected TIA referred to all the TIA clinics across the North West London region using a standard questionnaire. The population of the North West London region includes 2.4 million residents. This region includes five stroke centres with dedicated specialist TIA outpatient clinics based at the Charing Cross Hospital, Chelsea and Westminster Hospital, Hillingdon Hospital, Northwick Park Hospital and West Middlesex Hospital where almost all stroke and TIA patients are referred to by local General Practitioners (GPs) in the primary-care or Accident & Emergency Departments (A&Es). The questionnaire was sent to all National Health Service (NHS) TIA

clinical leads in the North West London region. The primary outcome measures of our survey questionnaire were the number of patients with suspected TIA consecutively referred to each of the TIA services of the North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020, the COVID-19 period, and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. Each TIA clinical lead was asked to provide the number of TIA referrals received in March and April 2019 and in March and April 2020. March 1, 2020 was selected as the start date of the COVID-19 period as the first case was documented in UK on February the 28<sup>th</sup>. All the TIA clinical leads received a prenotification letter that described the study and requested their participation. One week later, a second contact included a cover letter describing the study, assuring confidentiality, and providing instructions for completion of the survey and the survey instrument. In total, one reminder was sent to all the TIA clinical leads. No incentives were provided. We had a response rate of 100%. All data were entered into an electronic Excel database (Microsoft Corp, Redmond, Wash). Single data entry was used. Descriptive results are presented as percentage using Excel. No ethical approval was required for this type of research. In addition, no individual patient data were collected. Informed consent was not a legal requirement as the research was carried out using data collected as part of routine care and any researchers outside of the direct care team only had access to anonymised data.

## Results

Figure 1 shows the overall number of consecutive patients with suspect of TIA referred to the TIA services of the North West London region and the number of referrals received by each TIA centre between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. Collectively, during the COVID-19 period, the five TIA outpatient clinics of the North West London region received 440 referrals compared to 616 referrals received between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. This was associated with a fall in the number of the referrals by 28.6%. Of



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note, when we compared April 2020 with April 2019, the number of the referrals declined steeply by 40.1%. We documented also a 15.6% decrease in the number of the referrals received across the North West London region in March 2020 in contrast to March 2019, respectively 254 and 301. During the COVID-19 period Northwick Park Hospital and Chelsea and Westminster Hospital showed the most important decrease in the number of referrals to their TIA services, respectively 37.8% and 35.3%. The TIA service at Hillingdon Hospital was the only centre in North West London that demonstrated an overall increased number of referrals compared to same period in 2019. However, there was a 13.6% reduction in the number of patients referred to the TIA clinic at Hillingdon Hospital in April 2020 compared to April 2019.

**Discussion**

In this multicentre analysis we showed an overall reduction, between 18.8% and 37.8%, in the number of patients referred with suspected TIA to the specialised rapid outpatient clinics in the North West London region during the COVID-19 pandemic. To the authors’ knowledge, this is the first multi-centre report to document a significant decline of the referrals of patients with milder stroke symptoms to the TIA clinics of the same region during the COVID-19 pandemic. COVID-19 outbreak is having implications on stroke services in all parts of the world in terms of redeployment of stroke staff, reallocation of the stroke beds to COVID-19 patients and reduction of urgent interventions such as endovascular treatment and intravenous thrombolysis<sup>6</sup>. On the other hand, this pandemic has also largely impacted indirectly on the stroke care also in terms of sharp reduction of acute stroke admissions<sup>7</sup>. Our results highlight that patients, especially with milder stroke symptoms, may intentionally avoiding hospitals during the COVID-19 pandemic. Due to fears of infection, patients may now neglect milder stroke symptoms of a possible TIA to the point that they do not present to their local GPs in

the primary-care or A&Es while the reported incidence rate of more severe cerebrovascular events, such as ischemic stroke due to large vessel occlusion, remained stable during the COVID-19 pandemic as these more severe symptoms cannot be ignored by patients or family members<sup>7</sup>. If our findings will be confirmed in larger studies representing multiple populations, clinicians as well as patients and their family should be aware of the importance of early recognition and treatment of even milder stroke symptoms even in these difficult times. We are aware that our study has several limitations. Our study is limited by the retrospective design and our results reflect the trend in number of referrals to TIA clinics in a determined area which may not be generalised to all international healthcare practices some of which evaluate TIAs as inpatients. Finally, our findings are descriptive in nature and potential causes or confounders for the decreased number of referrals received by the TIA clinics during the COVID-19 pandemic were not explored (e.g. GPs are performing a more careful and thorough risk/benefit assessment of the appropriateness of their referral i.e. TIA versus mimics, given the risk of COVID-19 exposure).

## Summary/Conclusions

In conclusion, we believe that our multi-centre study provides further evidence of the impact of the COVID-19 pandemic on acute stroke services. Future studies and data acquisition of larger studies representing multiple populations are needed to confirm our findings and to better characterise the incidence of cerebrovascular disease during the COVID-19 pandemic.

## Acknowledgments

We would like to thank the entire medical and nurse staff of the TIA clinics at Charing Cross Hospital, Chelsea and Westminster Hospital, Hillingdon Hospital, Northwick Park Hospital and West Middlesex Hospital for their contribution.

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**Source of Funding**

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Disclosure of potential conflicts of interest:** Lucio D’Anna, Ambreen Ali Sheikh, Raj Bathula, Salwa Elmamoun, Adelaide Oppong, Singh Ravneeta, Rebecca Redwood, John Janssen, Soma Banerjee, Evangelos Vasileiadis.

**Data sharing statement**

The data that support the findings of this study are available from the corresponding author on reasonable request.

**References**

1. Lavallée PC, Meseguer E, Abboud H, Cabrejo L, Olivot JM, Simon O, et al. A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects. *Lancet Neurol.* 2007;
2. Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JN, et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. *Lancet.* 2007;
3. Cancelli I, Janes F, Gigli GL, Perelli A, Zanchettin B, Canal G, et al. Incidence of transient ischemic attack and early stroke risk: Validation of the ABCD2 score in an Italian population-based study. *Stroke.* 2011;42.

4. Brainin M. Stroke care and the COVID19 pandemic words from our President. 2020.
5. Teo K-C, Leung WCY, Wong Y-K, Liu RKC, Chan AHY, Choi OMY, et al. Delays in Stroke Onset to Hospital Arrival Time During COVID-19. *Stroke*. 2020;STROKEAHA120030105.
6. Markus HS, Brainin M. EXPRESS: COVID-19 and Stroke - A Global World Stroke Organisation perspective. *Int. J. Stroke*. 2020;0:174749302092347.
7. Siegler JEMD, Heslin MEBS, Thau LBS, Rn AS, Jovin TGMD. Falling stroke rates during COVID-19 pandemic at a Comprehensive Stroke Center: Cover title: Falling stroke rates during COVID-19. *J. Stroke Cerebrovasc. Dis.* [Internet]. 2020;104953. Available from: <https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104953>

### Figure legend

**Figure 1.** Numbers of patients with suspect of TIA referred overall to the TIA clinics of North West London region and to each hospital between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and 1<sup>st</sup> March to 30<sup>th</sup> April 2019.

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**Authors email address:**

- Lucio D’Anna: l.danna@imperial.ac.uk
- Ambreen Ali Sheikh: ambreen.alisheikh@nhs.net
- Raj Bathula: r.bathula@nhs.net
- Salwa Elmamoun: salwa.elmamoun@nhs.net
- Adelaide Oppong: Adelaide.Oppong@chelwest.nhs.uk
- Singh Ravneeta: Ravneeta.Singh@chelwest.nhs.uk
- Rebecca Redwood: Rebecca.Redwood@nhs.net
- John Janssen: john.janssen@nhs.net
- Soma Banerjee: Soma.Banerjee@nhs.net
- Evangelos Vasileiadis: evangelos.vasileiadis@nhs.net

**Author statement:**

- Lucio D’Anna: study concept, statistical analysis, drafting and critical revision of manuscript
- Ambreen Ali Sheikh: data collection, critical revision of manuscript
- Raj Bathula: data collection, critical revision of manuscript
- Salwa Elmamoun: data collection, critical revision of manuscript
- Adelaide Oppong: data collection, critical revision of manuscript
- Singh Ravneeta: data collection, critical revision of manuscript
- Rebecca Redwood: data collection, critical revision of manuscript
- John Janssen: data collection, critical revision of manuscript
- Soma Banerjee: data collection, critical revision of manuscript
- Evangelos Vasileiadis: study concept, drafting and critical revision of manuscript

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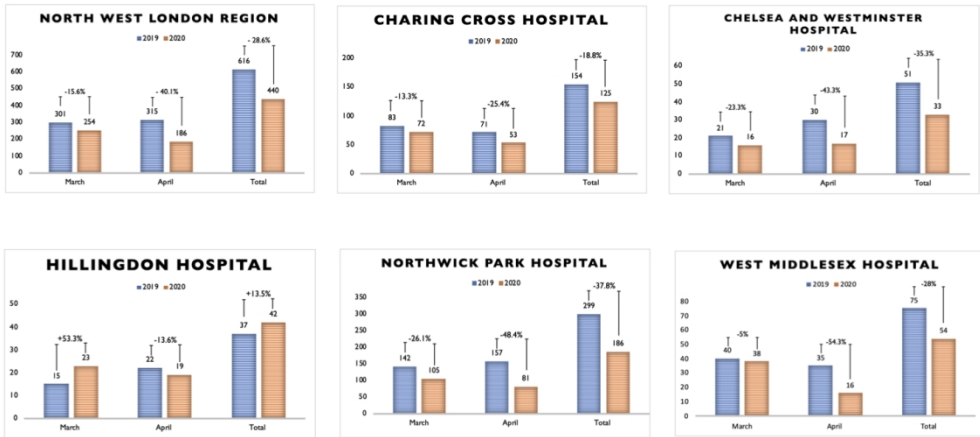


Figure 1. Numbers of patients with suspect of TIA referred overall to the TIA clinics of North West London region and to each hospital between 1st March to 30th April 2020 and 1st March to 30th April 2019.

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	<a href="#">#1</a> Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	1
<b>Abstract</b>		
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Problem formulation	<a href="#">#3</a> Description and significance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	4
Purpose or research question	<a href="#">#4</a> Purpose of the study and specific objectives or questions	4



Methods				
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	4	
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Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5	
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	5	
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Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	5	

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Data analysis	<a href="#">#14</a>	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	5
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Links to empirical data	<a href="#">#17</a>	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	5
<b>Discussion</b>			
Intergration with prior work, implications, transferability and contribution(s) to the field	<a href="#">#18</a>	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	6
Limitations	<a href="#">#19</a>	Trustworthiness and limitations of findings	6
<b>Other</b>			
Conflicts of interest	<a href="#">#20</a>	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	8
Funding	<a href="#">#21</a>	Sources of funding and other support; role of funders in data collection, interpretation and reporting	8

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## Decreasing referrals to Transient Ischemic Attack clinics during the COVID-19 outbreak. Results from a multi-centre cross-sectional survey.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-041514.R1
Article Type:	Original research
Date Submitted by the Author:	27-Jul-2020
Complete List of Authors:	D'Anna, Lucio; Imperial College London, Brain Sciences Sheikh, Ambreen; West Middlesex University Hospital, Stroke Bathula, Raj; Northwick Park Hospital, Stroke Elmamoun, Salwa; Chelsea and Westminster Healthcare NHS Trust, Stroke Oppong, Adelaide; Chelsea and Westminster Healthcare NHS Trust, Stroke Singh, Ravneeta; Chelsea and Westminster Healthcare NHS Trust, Stroke redwood, Rebecca; Chelsea and Westminster Healthcare NHS Trust, Stroke Janssen, John; Chelsea and Westminster Healthcare NHS Trust, Stroke Banerjee, Soma; Imperial College London, Brain Sciences vasileiadis, evangelos; Hillingdon Hospital, Stroke
<b>Primary Subject Heading</b>:	Neurology
Secondary Subject Heading:	Health services research
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# Decreasing referrals to Transient Ischemic Attack clinics during the COVID-19 outbreak.

## Results from a multi-centre cross-sectional survey.

Lucio D'Anna MD, PhD<sup>1,2</sup>, Ambreen Ali Sheikh MD<sup>3</sup>, Raj Bathula MD<sup>4</sup>, Salwa Elmamoun MD<sup>5</sup>, Adelaide Oppong MD<sup>5</sup>, Singh Ravneeta MD<sup>5</sup>, Rebecca Redwood MD<sup>5</sup>, John Janssen MD<sup>5</sup>, Soma Banerjee MD<sup>1,2</sup>, Evangelos Vasileiadis MD<sup>6</sup>.

<sup>1</sup>Department of Stroke and Neuroscience, Charing Cross Hospital, Imperial College London NHS Healthcare Trust, London, United Kingdom;

<sup>2</sup>Department of Brain Sciences, Imperial College London, London, United Kingdom;

<sup>3</sup>Stroke Centre, West Middlesex University Hospital, London, United Kingdom;

<sup>4</sup>Stroke Centre, Northwick Park Hospital, London, United Kingdom;

<sup>5</sup>Stroke Centre, Chelsea and Westminster Hospital, London, United Kingdom;

<sup>6</sup>Stroke Centre, Hillingdon Hospital, London, United Kingdom.

**Corresponding author:** Lucio D'Anna, Stroke Centre, Department of Stroke & Neurosciences, Charing Cross Hospital, Imperial College Healthcare NHS Trust, Fulham Palace Road, London W6 8RF, UK.

**Word count:** 1296

**Keywords:** COVID-19, transient ischemic attack, stroke prevention, TIA clinic

**Total number of tables and figures:** Figure 1

**Subject terms:** Transient Ischemic Attack

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**Abstract**

**Objective.** The COVID-19 pandemic is having major implications for stroke care with a documented significant fall in hospital acute stroke admissions. We investigated whether COVID-19 has resulted in a decreased number of referrals to the Transient Ischemic Attack (TIA) clinics across the North West London region.

**Setting and Design.** All the TIA clinical leads of the North West London region received an invitation by email to participate in an online survey in May 2020. The survey questionnaire aimed to assess the number of patients with suspected TIA consecutively referred to each of the TIA clinics of the North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020, the COVID-19 period, and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019.

**Results.** We had a response rate of 100%. During the COVID-19 period, the TIA clinics of the North West London region received 440 referrals compared to 616 referrals received between 1<sup>st</sup> March to 30<sup>th</sup> April 2019 with a fall in the number of the referrals by 28.6%. In April 2020 compared with April 2019, the number of the referrals declined by 40.1%.

**Conclusions.** This multicentre analysis documented a significant reduction in the number of patients referred with suspected TIA to the specialised rapid access outpatient clinics in the North West London region during the COVID-19 pandemic. Future studies are needed to confirm our findings and to better characterise the incidence of cerebrovascular disease during the COVID-19 pandemic.

### Strengths and Limitations of this study

- This is the first study investigating the effects of COVID-19 on the volume of patients presenting to Transient Ischemic Attack (TIA) clinics rather Stroke Units during the COVID-19 pandemic
- Response rate of 100%
- Reflection of results within the National Health Service in North West London region that might not be generalised to all international healthcare practices



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**Introduction**

Transient Ischemic Attack (TIA) is a common neurologic emergency that is strongly associated with a high early risk of subsequent stroke. Therefore, urgent assessment and management of patients in a dedicated TIA clinic is considered to be critical to reduce significantly the 90-day stroke risk by almost 80%<sup>1-3,4</sup>.Recent evidence showed that the number of patients attending the Emergency Department (ED) has significantly decreased<sup>5</sup> during the COVID-19 pandemic because of fear of contracting the infection<sup>6</sup>. In addition, the rate of non-respiratory hospital admissions for conditions such as acute coronary syndrome (ACS) sharply fell<sup>7</sup>. These observations suggested that some patients could have delayed the care for such conditions or died without seeking medical attention during the COVID-19 pandemic.

A recent survey of the World Stroke Organisation (WSO) across multiple countries including UK, Italy, Belgium, Greece, Iran, Chile and Colombia has documented that the COVID-19 pandemic has affected stroke care with a significant fall in the number of stroke admissions, up to 80%, during the COVID-19 outbreak<sup>8</sup>. Moreover, preliminary data suggested that a smaller proportion of patients with milder stroke symptoms presented to hospital during the COVID-19 pandemic<sup>9</sup>. However, to date, it is unclear if COVID-19 pandemic has impacted on the number of referrals to the TIA clinics. In this observational multi-centre survey, we compared the number of patients with suspected TIA referred to all the TIA clinics across the North West London region during the COVID-19 pandemic compared with a similar period in 2019.

**Methods**

We conducted a multi-centre, cross-sectional survey in May 2020 to assess the impact of the current COVID-19 pandemic on the number of patients with suspected TIA referred to all the TIA clinics across the North West London region using a standard questionnaire. The

population of the North West London region includes 2.4 million residents. This region includes five stroke centres with dedicated specialist TIA outpatient clinics based at the Charing Cross Hospital, Chelsea and Westminster Hospital, Hillingdon Hospital, Northwick Park Hospital and West Middlesex Hospital. In these centres almost all stroke and TIA patients are referred to by local General Practitioners (GPs) in the primary-care or Emergency Departments (ED). The referral pathway of patients with suspected TIA was unchanged in 2020 compared to 2019. The questionnaire was sent to all National Health Service (NHS) TIA clinical leads in the North West London region. The primary outcome measures of our survey questionnaire were the number of patients with suspected TIA consecutively referred to each of the TIA services of the North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020, the COVID-19 period, and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. Each TIA clinical lead was asked to provide the number of TIA referrals received in March and April 2019 and in March and April 2020. March 1, 2020 was selected as the start date of the COVID-19 period as the first case was documented in UK on February the 28<sup>th</sup>. All the TIA clinical leads received a prenotification letter that described the study and requested their participation. One week later, a second contact included a cover letter describing the study, assuring confidentiality, and providing instructions for completion of the survey and the survey instrument. In total, one reminder was sent to all the TIA clinical leads. No incentives were provided. We had a response rate of 100%. All data were entered into an electronic Excel database (Microsoft Corp, Redmond, Wash). Single data entry was used. Descriptive results are presented as percentage using Excel. No ethical approval was required for this type of research. In addition, no individual patient data were collected. Informed consent was not a legal requirement as the research was carried out using data collected as part of routine care and any researchers outside of the direct care team only had access to anonymised data.

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*Patient and Public Involvement*

No patient involved

**Results**

Figure 1 and Table 1 show the overall number of consecutive patients with suspected TIA referred to the TIA services of the North West London region and the number of referrals received by each TIA centre between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. Collectively, during the COVID-19 period, the five TIA outpatient clinics of the North West London region received 440 referrals compared to 616 referrals received between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. This was associated with a fall in the number of the referrals by 28.6%. Of note, when we compared April 2020 with April 2019, the number of the referrals declined steeply by 40.1%. We also documented a 15.6% decrease in the number of referrals received across the North West London region in March 2020 in contrast to March 2019, respectively 254 and 301. During the COVID-19 period Northwick Park Hospital and Chelsea and Westminster Hospital showed the greatest decline in the number of referrals to their TIA services, respectively 37.8% and 35.3%. The TIA service at Hillingdon Hospital was the only centre in North West London that demonstrated an overall increased number of referrals compared to same period in 2019. However, there was a 13.6% reduction in the number of patients referred to the TIA clinic at Hillingdon Hospital in April 2020 compared to April 2019.

## Discussion

In this multicentre analysis we showed an overall reduction, between 18.8% and 37.8%, in the number of patients referred with suspected TIA to the specialised rapid access outpatient clinics in the North West London region during the COVID-19 pandemic.

To the authors' knowledge, this is the first multi-centre report to document a significant decline in the referrals of patients with milder stroke symptoms to the TIA clinics of the same region during the COVID-19 pandemic. The COVID-19 outbreak is having implications on stroke services in all parts of the world in terms of redeployment of stroke staff, re-allocation of the stroke beds for COVID-19 patients and reduction of urgent interventions such as endovascular treatment and intravenous thrombolysis<sup>10</sup>. On the other hand, this pandemic has also largely impacted indirectly on the stroke care also in terms of sharp decline in acute stroke admissions<sup>11,4</sup>.

Our results highlight that patients, especially those with milder stroke symptoms, may have intentionally avoided hospitals during the COVID-19 pandemic. Due to fears of infection, patients may now neglect milder stroke symptoms of a possible TIA to the point that they do not present to their local GPs in the primary-care or EDs while the reported incidence rate of more severe cerebrovascular events, such as ischemic stroke due to large vessel occlusion, remained stable during the COVID-19 pandemic as these more severe symptoms are less likely to be ignored by patients or family members<sup>11</sup>. Clinicians as well as patients and their family should be aware of the importance of early recognition and treatment of even milder stroke symptoms even in these difficult times.

We are aware that our study has several limitations. Our study is limited by the retrospective design and our results reflect the trend in number of referrals to TIA clinics in a determined

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area which may not be generalised to all international healthcare practices some of which evaluate TIAs as inpatients. Finally, our findings are descriptive in nature and potential causes or confounders for the decreased number of referrals received by the TIA clinics during the COVID-19 pandemic were not explored (e.g. GPs are performing a more careful and thorough risk/benefit assessment of the appropriateness of their referral i.e. TIA versus mimics, given the risk of COVID-19 exposure).

**Summary/Conclusions**

In conclusion, we believe that our multi-centre study provides further evidence of the impact of the COVID-19 pandemic on acute stroke services. Future studies and data acquisition from larger studies representing multiple populations are needed to confirm our findings and to better characterise the incidence of cerebrovascular disease during the COVID-19 pandemic.

**Acknowledgments**

We would like to thank the entire medical and nursing staff of the TIA clinics at Charing Cross Hospital, Chelsea and Westminster Hospital, Hillingdon Hospital, Northwick Park Hospital and West Middlesex Hospital for their contribution.

**Source of Funding**

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interest.** Lucio D’Anna, Ambreen Ali Sheikh, Raj Bathula, Salwa Elmamoun, Adelaide Oppong, Singh Ravneeta, Rebecca Redwood, John Janssen, Soma Banerjee, Evangelos Vasileiadis: none declared

### Data sharing statement

The data that support the findings of this study are available from the corresponding author on reasonable request.

### References

1. Lavallée PC, Meseguer E, Abboud H, Cabrejo L, Olivot JM, Simon O, et al. A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects. *Lancet Neurol.* 2007;
2. Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JN, et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. *Lancet.* 2007;
3. Cancelli I, Janes F, Gigli GL, Perelli A, Zanchettin B, Canal G, et al. Incidence of transient ischemic attack and early stroke risk: Validation of the ABCD2 score in an Italian population-based study. *Stroke.* 2011;42.
4. Saban M, Reznik A, Shachar T, Sivan-Hoffmann R. Reduction in stroke patients’ referral to the ED in the COVID-19 era: A four-year comparative study. *medRxiv.* 2020;
5. Hartnett KP, Kite-Powell A, DeVies J, Coletta MA, Boehmer TK, Adjemian J, et al. Impact of the COVID-19 Pandemic on Emergency Department Visits - United States,

January 1, 2019-May 30, 2020. *MMWR. Morb. Mortal. Wkly. Rep.* 2020;

6. Laura E. Wong; MD; PhD; Jessica E. Hawkins; MEd; Simone Langness; Karen L. Murrell; Patricia Iris; MD & Amanda Sammann; MPH. Where Are All the Patients? Addressing Covid-19 Fear to Encourage Sick Patients to Seek Emergency Care. *NEJM Catal.* 2020;

7. De Filippo O, D’Ascenzo F, Angelini F, Bocchino PP, Conrotto F, Saglietto A, et al. Reduced Rate of Hospital Admissions for ACS during Covid-19 Outbreak in Northern Italy. *N. Engl. J. Med.* 2020;

8. Brainin M. Stroke care and the COVID19 pandemic words from our President. 2020.

9. Teo K-C, Leung WCY, Wong Y-K, Liu RKC, Chan AHY, Choi OMY, et al. Delays in Stroke Onset to Hospital Arrival Time During COVID-19. *Stroke.* 2020;STROKEAHA120030105.

10. Markus HS, Brainin M. EXPRESS: COVID-19 and Stroke - A Global World Stroke Organisation perspective. *Int. J. Stroke.* 2020;0:174749302092347.

11. Siegler JEMD, Heslin MEBS, Thau LBS, Rn AS, Jovin TGMD. Falling stroke rates during COVID-19 pandemic at a Comprehensive Stroke Center: Cover title: Falling stroke rates during COVID-19. *J. Stroke Cerebrovasc. Dis.* [Internet]. 2020;104953. Available from: <https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104953>

**Figure legend**

**Figure 1.** Numbers of patients with suspect of TIA referred overall to the TIA clinics of North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and 1<sup>st</sup> March to 30<sup>th</sup> April 2019.

**Table 1. Numbers of patients with suspect of TIA referred each of the TIA clinics of North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and 1<sup>st</sup> March to 30<sup>th</sup> April 2019.**

	<b>Charing Cross Hospital</b>	<b>Chelsea and Westminster Hospital</b>	<b>Hillingdon Hospital</b>	<b>Northwick Park Hospital</b>	<b>West Middlesex Hospital</b>
<b><i>March 2019 (n)</i></b>	83	21	15	142	40
<b><i>March 2020 (n)</i></b>	72	16	23	105	38
<b><i>Difference, %</i></b>	-13.3%	-23.3%	+53.3%	-26.1%	-5%
<b><i>April 2019 (n)</i></b>	71	30	22	157	35
<b><i>April 2020 (n)</i></b>	53	17	19	81	16
<b><i>Difference, %</i></b>	-25.4%	-43.3%	-13.6%	-48.4%	-54.3%
<b><i>Total 2019 (n)</i></b>	154	51	37	299	75
<b><i>Total 2020 (n)</i></b>	125	33	42	186	54
<b><i>Difference, %</i></b>	-18.8%	-35.3%	+13.5%	-37.8%	-28%



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**Authors email address:**

Lucio D’Anna: l.danna@imperial.ac.uk

Ambreen Ali Sheikh: ambreen.alisheikh@nhs.net

Raj Bathula: r.bathula@nhs.net

Salwa Elmamoun: salwa.elmamoun@nhs.net

Adelaide Oppong: Adelaide.Oppong@chelwest.nhs.uk

Singh Ravneeta: Ravneeta.Singh@chelwest.nhs.uk

Rebecca Redwood: Rebecca.Redwood@nhs.net

John Janssen: john.janssen@nhs.net

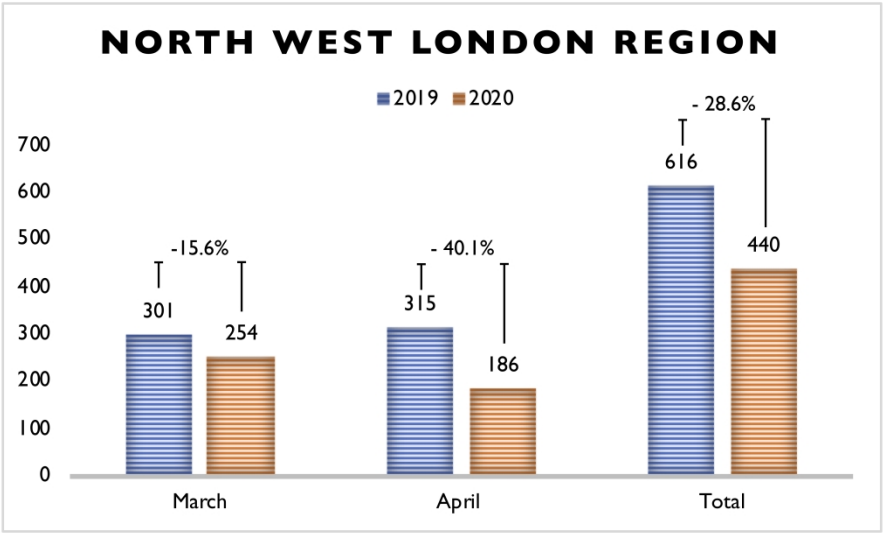
Soma Banerjee: Soma.Banerjee@nhs.net

Evangelos Vasileiadis: evangelos.vasileiadis@nhs.net

**Author statement:**

- Lucio D’Anna: study concept, statistical analysis, drafting and critical revision of manuscript
- Ambreen Ali Sheikh: data collection, critical revision of manuscript
- Raj Bathula: data collection, critical revision of manuscript
- Salwa Elmamoun: data collection, critical revision of manuscript
- Adelaide Oppong: data collection, critical revision of manuscript
- Singh Ravneeta: data collection, critical revision of manuscript
- Rebecca Redwood: data collection, critical revision of manuscript
- John Janssen: data collection, critical revision of manuscript
- Soma Banerjee: data collection, critical revision of manuscript
- Evangelos Vasileiadis: study concept, drafting and critical revision of manuscript

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# Reporting checklist for qualitative study.

Based on the SRQR guidelines.

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		Page Number
Reporting Item		
<b>Title</b>		
<a href="#">#1</a> Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended		1
<b>Abstract</b>		
<a href="#">#2</a> Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions		2
<b>Introduction</b>		
Problem formulation	<a href="#">#3</a> Description and significance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	4
Purpose or research question	<a href="#">#4</a> Purpose of the study and specific objectives or questions	4

Methods				
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	4	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	4	
Context	#7	Setting / site and salient contextual factors; rationale	4	
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5	
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	5	
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	5	
Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	5	

Units of study	<a href="#">#12</a>	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	<a href="#">#13</a>	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	5
Data analysis	<a href="#">#14</a>	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	5
Techniques to enhance trustworthiness	<a href="#">#15</a>	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	5
<b>Results/findings</b>			
Syntheses and interpretation	<a href="#">#16</a>	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	5
Links to empirical data	<a href="#">#17</a>	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	5
<b>Discussion</b>			
Intergration with prior work, implications, transferability and contribution(s) to the field	<a href="#">#18</a>	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	6
Limitations	<a href="#">#19</a>	Trustworthiness and limitations of findings	6
<b>Other</b>			
Conflicts of interest	<a href="#">#20</a>	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	8
Funding	<a href="#">#21</a>	Sources of funding and other support; role of funders in data collection, interpretation and reporting	8

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## Decreasing referrals to Transient Ischemic Attack clinics during the COVID-19 outbreak. Results from a multi-centre cross-sectional survey.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-041514.R2
Article Type:	Original research
Date Submitted by the Author:	29-Aug-2020
Complete List of Authors:	D'Anna, Lucio; Imperial College London, Brain Sciences Sheikh, Ambreen; West Middlesex University Hospital, Stroke Bathula, Raj; Northwick Park Hospital, Stroke Elmamoun, Salwa; Chelsea and Westminster Healthcare NHS Trust, Stroke Oppong, Adelaide; Chelsea and Westminster Healthcare NHS Trust, Stroke Singh, Ravneeta; Chelsea and Westminster Healthcare NHS Trust, Stroke redwood, Rebecca; Chelsea and Westminster Healthcare NHS Trust, Stroke Janssen, John; Chelsea and Westminster Healthcare NHS Trust, Stroke Banerjee, Soma; Imperial College London, Brain Sciences vasileiadis, evangelos; Hillingdon Hospital, Stroke
<b>Primary Subject Heading</b>:	Neurology
Secondary Subject Heading:	Health services research
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# Decreasing referrals to Transient Ischemic Attack clinics during the COVID-19 outbreak.

## Results from a multi-centre cross-sectional survey.

Lucio D'Anna MD, PhD<sup>1,2</sup>, Ambreen Ali Sheikh MD<sup>3</sup>, Raj Bathula MD<sup>4</sup>, Salwa Elmamoun MD<sup>5</sup>, Adelaide Oppong MD<sup>5</sup>, Singh Ravneeta MD<sup>5</sup>, Rebecca Redwood MD<sup>5</sup>, John Janssen MD<sup>5</sup>, Soma Banerjee MD<sup>1,2</sup>, Evangelos Vasileiadis MD<sup>6</sup>.

<sup>1</sup>Department of Stroke and Neuroscience, Charing Cross Hospital, Imperial College London NHS Healthcare Trust, London, United Kingdom;

<sup>2</sup>Department of Brain Sciences, Imperial College London, London, United Kingdom;

<sup>3</sup>Stroke Centre, West Middlesex University Hospital, London, United Kingdom;

<sup>4</sup>Stroke Centre, Northwick Park Hospital, London, United Kingdom;

<sup>5</sup>Stroke Centre, Chelsea and Westminster Hospital, London, United Kingdom;

<sup>6</sup>Stroke Centre, Hillingdon Hospital, London, United Kingdom.

**Corresponding author:** Lucio D'Anna, Stroke Centre, Department of Stroke & Neurosciences, Charing Cross Hospital, Imperial College Healthcare NHS Trust, Fulham Palace Road, London W6 8RF, UK; email address: l.danna@imperial.ac.uk

**Word count:** 1482

**Keywords:** COVID-19, transient ischemic attack, stroke prevention, TIA clinic

**Total number of tables and figures:** Figure 1

**Subject terms:** Transient Ischemic Attack

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**Abstract**

**Objective.** The COVID-19 pandemic is having major implications for stroke care with a documented significant fall in hospital acute stroke admissions. We investigated whether COVID-19 has resulted in a decreased number of referrals to the Transient Ischemic Attack (TIA) clinics across the North West London region.

**Setting and Design.** All the TIA clinical leads of the North West London region received an invitation by email to participate in an online survey in May 2020. The survey questionnaire aimed to assess the number of patients with suspected TIA consecutively referred to each of the TIA clinics of the North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020, the COVID-19 period, and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019.

**Results.** We had a response rate of 100%. During the COVID-19 period, the TIA clinics of the North West London region received 440 referrals compared to 616 referrals received between 1<sup>st</sup> March to 30<sup>th</sup> April 2019 with a fall in the number of the referrals by 28.6%. In April 2020 compared with April 2019, the number of the referrals declined by 40.1%.

**Conclusions.** This multicentre analysis documented a significant reduction in the number of patients referred with suspected TIA to the specialised rapid access outpatient clinics in the North West London region during the COVID-19 pandemic. Future studies are needed to confirm our findings and to better characterise the incidence of cerebrovascular disease during the COVID-19 pandemic.

### Strengths and Limitations of this study

- This is the first study investigating the effects of COVID-19 on the volume of patients presenting to Transient Ischemic Attack (TIA) clinics rather Stroke Units during the COVID-19 pandemic
- Response rate of 100%
- Reflection of results within the National Health Service in North West London region that might not be generalised to all international healthcare practices

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**Introduction**

Transient Ischemic Attack (TIA) is a common neurologic emergency that is strongly associated with a high early risk of subsequent stroke. Therefore, urgent assessment and management of patients in a dedicated TIA clinic is considered to be critical to reduce significantly the 90-day stroke risk by almost 80%<sup>1-3,4</sup>.Recent evidence showed that the number of patients attending the Emergency Department (ED) has significantly decreased<sup>5</sup> during the COVID-19 pandemic because of fear of contracting the infection<sup>6</sup>. In addition, the rate of non-respiratory hospital admissions for conditions such as acute coronary syndrome (ACS) sharply fell<sup>7</sup>. These observations suggested that some patients could have delayed the care for such conditions or died without seeking medical attention during the COVID-19 pandemic.

A recent survey of the World Stroke Organisation (WSO) across multiple countries including UK, Italy, Belgium, Greece, Iran, Chile and Colombia has documented that the COVID-19 pandemic has affected stroke care with a significant fall in the number of stroke admissions, up to 80%, during the COVID-19 outbreak<sup>8</sup>. Moreover, preliminary data suggested that a smaller proportion of patients with milder stroke symptoms presented to hospital during the COVID-19 pandemic<sup>9</sup>. However, to date, it is unclear if COVID-19 pandemic has impacted on the number of referrals to the TIA clinics. In this observational multi-centre survey, we compared the number of patients with suspected TIA referred to all the TIA clinics across the North West London region during the COVID-19 pandemic compared with a similar period in 2019.

**Methods**

We conducted a multi-centre, cross-sectional survey in May 2020 to assess the impact of the current COVID-19 pandemic on the number of patients with suspected TIA referred to all the TIA clinics across the North West London region using a standard questionnaire. The

population of the North West London region includes 2.4 million residents. This region includes five stroke centres with dedicated specialist TIA outpatient clinics based at the Charing Cross Hospital, Chelsea and Westminster Hospital, Hillingdon Hospital, Northwick Park Hospital and West Middlesex Hospital. In these centres almost all stroke and TIA patients are referred to by local General Practitioners (GPs) in the primary-care or Emergency Departments (ED). The referral pathway of patients with suspected TIA was unchanged in 2020 compared to 2019. The questionnaire was sent to all National Health Service (NHS) TIA clinical leads in the North West London region. The survey that was sent to all the five TIA clinical leads asked the following questions: 1) What is the number of patients with suspected TIA referred to your TIA clinic service between 1<sup>st</sup> and 31<sup>st</sup> March 2019?; 2) What is the number of patients with suspected TIA referred to your TIA clinic service between 1<sup>st</sup> and 31<sup>st</sup> March 2020?; 3) What is the number of patients with suspected TIA referred to your TIA clinic service between 1<sup>st</sup> and 30<sup>th</sup> April 2019?; 4) What is the number of patients with suspected TIA referred to your TIA clinic service between 1<sup>st</sup> and 30<sup>th</sup> April 2020?. The primary outcome measures of our survey questionnaire were the number of patients with suspected TIA consecutively referred to each of the TIA services of the North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020, the COVID-19 period, and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. Each TIA clinical lead was asked to provide the number of TIA referrals received in March and April 2019 and in March and April 2020. March 1, 2020 was selected as the start date of the COVID-19 period as the first case was documented in UK on February the 28<sup>th</sup>. Each TIA clinical lead provided data on consecutive eligible patients referred to their service by using a databank of admissions that is used for reporting to a central UK stroke data bank Sentinel Stroke National Audit Programme (SSNAP). Electronic and paper based medical records of eligible patients were retrieved from each hospital medical archive. This survey was carried out using data collected as part of routine care and any researchers outside of the direct care

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team only had access to anonymised data. All the TIA clinical leads received a prenotification letter that described the study and requested their participation. One week later, a second contact included a cover letter describing the study, assuring confidentiality, and providing instructions for completion of the survey and the survey instrument. In total, one reminder was sent to all the TIA clinical leads. No incentives were provided. We had a response rate of 100%. All data were entered into an electronic Excel database (Microsoft Corp, Redmond, Wash). Single data entry was used. Descriptive results are presented as percentage using Excel. No ethical approval was required for this type of research. In addition, no individual patient data were collected. Informed consent was not a legal requirement as the research was carried out using data collected as part of routine care and any researchers outside of the direct care team only had access to anonymised data.

*Patient and Public Involvement*

No patient involved

**Results**

Figure 1 and Table 1 show the overall number of consecutive patients with suspected TIA referred to the TIA services of the North West London region and the number of referrals received by each TIA centre between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. Collectively, during the COVID-19 period, the five TIA outpatient clinics of the North West London region received 440 referrals compared to 616 referrals received between 1<sup>st</sup> March to 30<sup>th</sup> April 2019. This was associated with a fall in the number of the referrals by 28.6%. Of note, when we compared April 2020 with April 2019, the number of the referrals declined steeply by 40.1%. We also documented a 15.6% decrease in the number of referrals received across the North West London region in March 2020 in contrast to March

2019, respectively 254 and 301. During the COVID-19 period Northwick Park Hospital and Chelsea and Westminster Hospital showed the greatest decline in the number of referrals to their TIA services, respectively 37.8% and 35.3%. The TIA service at Hillingdon Hospital was the only centre in North West London that demonstrated an overall increased number of referrals compared to same period in 2019. However, there was a 13.6% reduction in the number of patients referred to the TIA clinic at Hillingdon Hospital in April 2020 compared to April 2019.

## Discussion

In this multicentre analysis we showed an overall reduction, between 18.8% and 37.8%, in the number of patients referred with suspected TIA to the specialised rapid access outpatient clinics in the North West London region during the COVID-19 pandemic.

To the authors' knowledge, this is the first multi-centre report to document a significant decline in the referrals of patients with milder stroke symptoms to the TIA clinics of the same region during the COVID-19 pandemic. The COVID-19 outbreak is having implications on stroke services in all parts of the world in terms of redeployment of stroke staff, re-allocation of the stroke beds for COVID-19 patients and reduction of urgent interventions such as endovascular treatment and intravenous thrombolysis<sup>10</sup>. On the other hand, this pandemic has also largely impacted indirectly on the stroke care also in terms of sharp decline in acute stroke admissions<sup>11,4</sup>.

Our results highlight that patients, especially those with milder stroke symptoms, may have intentionally avoided hospitals during the COVID-19 pandemic. Due to fears of infection, patients may now neglect milder stroke symptoms of a possible TIA to the point that they do not present to their local GPs in the primary-care or EDs while the reported incidence rate of



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more severe cerebrovascular events, such as ischemic stroke due to large vessel occlusion, remained stable during the COVID-19 pandemic as these more severe symptoms are less likely to be ignored by patients or family members<sup>11</sup>. Clinicians as well as patients and their family should be aware of the importance of early recognition and treatment of even milder stroke symptoms even in these difficult times.

We are aware that our study has several limitations. Our study is limited by the retrospective design and our results reflect the trend in number of referrals to TIA clinics in a determined area which may not be generalised to all international healthcare practices some of which evaluate TIAs as inpatients. Finally, our findings are descriptive in nature and potential causes or confounders for the decreased number of referrals received by the TIA clinics during the COVID-19 pandemic were not explored (e.g. GPs are performing a more careful and thorough risk/benefit assessment of the appropriateness of their referral i.e. TIA versus mimics, given the risk of COVID-19 exposure).

**Summary/Conclusions**

In conclusion, we believe that our multi-centre study provides further evidence of the impact of the COVID-19 pandemic on acute stroke services. Future studies and data acquisition from larger studies representing multiple populations are needed to confirm our findings and to better characterise the incidence of cerebrovascular disease during the COVID-19 pandemic.

**Acknowledgments**

We would like to thank the entire medical and nursing staff of the TIA clinics at Charing Cross Hospital, Chelsea and Westminster Hospital, Hillingdon Hospital, Northwick Park Hospital and West Middlesex Hospital for their contribution.

### Source of Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interest.** Lucio D'Anna, Ambreen Ali Sheikh, Raj Bathula, Salwa Elmamoun, Adelaide Oppong, Singh Ravneeta, Rebecca Redwood, John Janssen, Soma Banerjee, Evangelos Vasileiadis: none declared

### Data sharing statement

The data that support the findings of this study are available from the corresponding author on reasonable request.

### References

1. Lavallée PC, Meseguer E, Abboud H, Cabrejo L, Olivot JM, Simon O, et al. A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects. *Lancet Neurol.* 2007;
2. Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JN, et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. *Lancet.* 2007;

3. Cancelli I, Janes F, Gigli GL, Perelli A, Zanchettin B, Canal G, et al. Incidence of transient ischemic attack and early stroke risk: Validation of the ABCD2 score in an Italian population-based study. *Stroke*. 2011;42.

4. Saban M, Reznik A, Shachar T, Sivan-Hoffmann R. Reduction in stroke patients' referral to the ED in the COVID-19 era: A four-year comparative study. *medRxiv*. 2020;

5. Hartnett KP, Kite-Powell A, DeVies J, Coletta MA, Boehmer TK, Adjemian J, et al. Impact of the COVID-19 Pandemic on Emergency Department Visits - United States, January 1, 2019-May 30, 2020. *MMWR. Morb. Mortal. Wkly. Rep*. 2020;

6. Laura E. Wong; MD; PhD; Jessica E. Hawkins; MEd; Simone Langness; Karen L. Murrell; Patricia Iris; MD & Amanda Sammann; MPH. Where Are All the Patients? Addressing Covid-19 Fear to Encourage Sick Patients to Seek Emergency Care. *NEJM Catal*. 2020;

7. De Filippo O, D'Ascenzo F, Angelini F, Bocchino PP, Conrotto F, Saglietto A, et al. Reduced Rate of Hospital Admissions for ACS during Covid-19 Outbreak in Northern Italy. *N. Engl. J. Med*. 2020;

8. Brainin M. Stroke care and the COVID19 pandemic words from our President. 2020.

9. Teo K-C, Leung WCY, Wong Y-K, Liu RKC, Chan AHY, Choi OMY, et al. Delays in Stroke Onset to Hospital Arrival Time During COVID-19. *Stroke*. 2020;STROKEAHA120030105.

10. Markus HS, Brainin M. EXPRESS: COVID-19 and Stroke - A Global World Stroke Organisation perspective. *Int. J. Stroke*. 2020;0:174749302092347.

11. Siegler JEMD, Heslin MEBS, Thau LBS, Rn AS, Jovin TGMD. Falling stroke rates during COVID-19 pandemic at a Comprehensive Stroke Center: Cover title: Falling stroke rates during COVID-19. *J. Stroke Cerebrovasc. Dis*. [Internet]. 2020;104953.

Available from: <https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104953>

## Figure legend

**Figure 1.** Numbers of patients with suspect of TIA referred overall to the TIA clinics of North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and 1<sup>st</sup> March to 30<sup>th</sup> April 2019.

**Table 1.** Numbers of patients with suspect of TIA referred each of the TIA clinics of North West London region between 1<sup>st</sup> March to 30<sup>th</sup> April 2020 and 1<sup>st</sup> March to 30<sup>th</sup> April 2019.

	Charing Cross Hospital	Chelsea and Westminster Hospital	Hillingdon Hospital	Northwick Park Hospital	West Middlesex Hospital
<i>March 2019 (n)</i>	83	21	15	142	40
<i>March 2020 (n)</i>	72	16	23	105	38
<i>Difference, %</i>	-13.3%	-23.3%	+53.3%	-26.1%	-5%
<i>April 2019 (n)</i>	71	30	22	157	35
<i>April 2020 (n)</i>	53	17	19	81	16
<i>Difference, %</i>	-25.4%	-43.3%	-13.6%	-48.4%	-54.3%
<i>Total 2019 (n)</i>	154	51	37	299	75

<b>Total 2020 (n)</b>	125	33	42	186	54
<b>Difference, %</b>	-18.8%	-35.3%	+13.5%	-37.8%	-28%

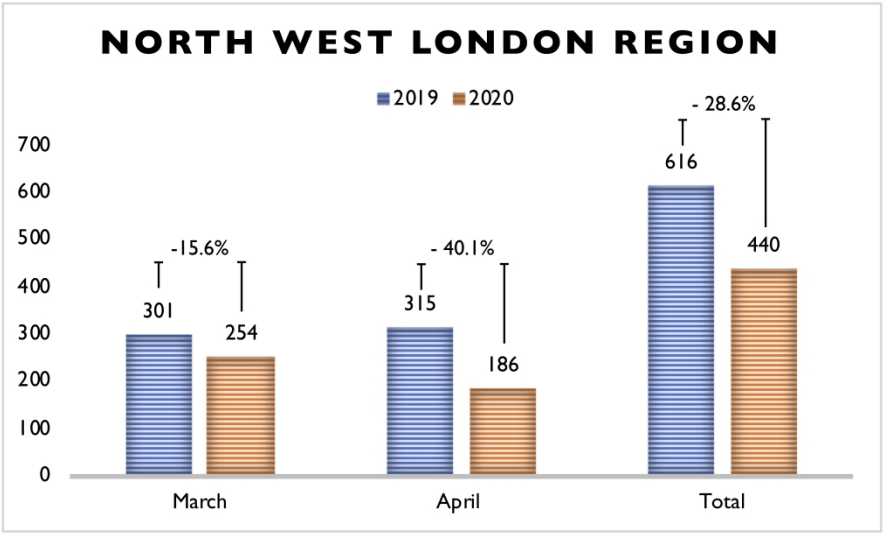
**Authors email address:**

- Lucio D’Anna: l.danna@imperial.ac.uk
- Ambreen Ali Sheikh: ambreen.alisheikh@nhs.net
- Raj Bathula: r.bathula@nhs.net
- Salwa Elmamoun: salwa.elmamoun@nhs.net
- Adelaide Oppong: Adelaide.Oppong@chelwest.nhs.uk
- Singh Ravneeta: Ravneeta.Singh@chelwest.nhs.uk
- Rebecca Redwood: Rebecca.Redwood@nhs.net
- John Janssen: john.janssen@nhs.net
- Soma Banerjee: Soma.Banerjee@nhs.net
- Evangelos Vasileiadis: evangelos.vasileiadis@nhs.net

**Author statement:**

- Lucio D’Anna: study concept, statistical analysis, drafting and critical revision of manuscript
- Ambreen Ali Sheikh: data collection, critical revision of manuscript
- Raj Bathula: data collection, critical revision of manuscript

- Salwa Elmamoun: data collection, critical revision of manuscript
- Adelaide Oppong: data collection, critical revision of manuscript
- Singh Ravneeta: data collection, critical revision of manuscript
- Rebecca Redwood: data collection, critical revision of manuscript
- John Janssen: data collection, critical revision of manuscript
- Soma Banerjee: data collection, critical revision of manuscript
- Evangelos Vasileiadis: study concept, drafting and critical revision of manuscript



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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found (page 2)
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (page 4)
Objectives	3	State specific objectives, including any prespecified hypotheses (page 4)
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper (page 4 and 5)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (page 4 and 5)
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants (page 4 and 5)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (page 4 and 5)
Bias	9	Describe any efforts to address potential sources of bias (page 4 and 5)
Study size	10	Explain how the study size was arrived at (page 4 and 5)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (page 4 and 5)
Statistical methods (page 5)	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
<b>Results</b>		
Participants Page 6	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data Page 6	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest
Outcome data Page 6	15*	Report numbers of outcome events or summary measures
Main results Page 6	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a



		meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results page 7	18	Summarise key results with reference to study objectives
Limitations page 7 and 8	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation page 7	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability page 7 and 8	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
Funding page 8	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).